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## HCV and Work Ability Assessment

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### Abstract

Modifications to work and work ability assessment are required to prevent occupational transmission of hepatitis C virus (HCV). This is usually required in the health care setting, where exposure-prone procedures (EPPs) should not be carried out by infectious carriers of HCV. The risk of an individual surgeon acquiring HCV has been estimated at 0.001–0.032% per annum. Even in an area with a high prevalence of HCV among its population, the risk of acquiring HCV through occupational exposure is low. Rates of viral clearance with treatment of acute HCV infection are considerably higher than treatment of chronic HCV infection. Consequently, it is imperative that health care workers follow universal precautions and promptly report all exposures to blood or body fluid exposures according to their local policy. Health care workers who embark on, or transfer to, a career that requires EPP (exposure-prone procedures and dialysis work) should be assessed to ensure that they are free from infection with HCV. If the HCV antibodies are positive, the health care worker should be tested for HCV RNA PCR. If the HCV RNA PCR is negative on two separate occasions, the health care worker may be permitted to perform EPPs. If the HCV RNA PCR is positive, the health care worker should not be allowed to perform EPPs. Health care workers who already perform EPPs and who believe they may have been exposed to HCV infection should be advised to seek advice from their occupational health department for confidential advice on whether they should be tested.

**Keywords:** HCV, work ability assessment, fitness for work

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## 1. Introduction

Work ability assessment or fitness to work refers to the process of ensuring that an employee can complete a task safely without presenting a risk to themselves, their colleagues, the company, or a third party. This term also refers to the impact of sickness and absence of employees in order to assess the possibility of having an employee return to work quickly and safely.

Work ability assessments are most often performed to determine medical fitness after an illness or injury, sometimes at the request of an employer after an offer of employment or as a condition of a job transfer.

Fitness to work assesses the capacity of an individual to perform physical and psychological work tasks according to the demands of the job. This demand may be directly associated with a task (e.g., carrying loads) or may be associated with a location that will impact the individual's health. Therefore, fitness to work addresses both the task and the location of the work to be done.

Reduced work productivity (WP) is a measure of the impact of illness and treatment burden in patients diagnosed with chronic diseases [1]. Patient's WP in the setting of a chronic condition presents a complex phenomenon that cannot be understood only by obtaining patient's clinical information. It is also important to collect patient-reported outcomes, especially ones that capture patients' energy and physical components. Hepatitis C (HCV) infection has a considerable negative impact on patient-reported outcomes (PRO) and patients' WP [2]. Numerous manifestations of HCV lead to an economic burden related to the complications and extrahepatic manifestation, thus decreasing WP [3]. For that reason, it is important to collect information that can help caregivers to develop a plan for maintaining patients' employment. Targeting important aspects of PROs has a substantial positive impact on patients' well-being as well as their WP, which results in notable economic benefits for the whole society [4].

## **2. Impact of HCV infection on work ability and productivity**

Chronic HCV is a global health problem affecting 130–170 million people worldwide (80% of patients with acute HCV infections will develop chronic HCV). Every year, 3–4 million people are infected, and approximately 9 million patients have HCV infection in Europe, with greater prevalence in the southern and eastern European regions [5]. Around 2.7–4.1 million people have chronic HCV (HCV) in the United States. While frequently believed of as an asymptomatic disease, numerous studies have shown that those with chronic HCV experience increased work impairment revealed as decreased WP and increased absenteeism and presenteeism (attending work while being impaired) [6]. Risk factors identified included blood transfusion, injection drug use, employment in patient care or clinical laboratory work, exposure to a sex partner or household member who has had a history of hepatitis, exposure to multiple sex partners, and low socioeconomic level. These studies reported no association with military service or exposures resulting from medical, surgical, or dental procedures, tattooing, acupuncture, ear piercing, or foreign travel. If transmission from such exposures does occur, the frequency might be too low to detect [7].

Working in the health care, emergency medical (e.g., emergency medical technicians and paramedics), and public safety sectors (e.g., fire-service, law-enforcement, and correctional facility personnel) who have exposure to blood in the workplace are at high risk for being infected with bloodborne pathogens. Nevertheless, occurrence of HCV infection among health-care workers, including surgeons, is no greater than the general population, averaging 1–2%, and

is 10 times lower than that for HBV infection [8]. In a single study that evaluated risk factors for infection, a history of unintentional needle-stick injury was the only occupational risk factor independently associated with HCV infection [9].

Among health care workers, the prevalence of HCV infection is about the same as that of the general population: 1.5%. Following percutaneous exposure of health care workers to infected blood, the risk of HCV seroconversion ranges from 0 to 10%, with an average of 1.8% [7].

HCV infection is a major cause of fatigue, muscle and joint pain, depression, and other psychological disorders, which decrease patient health-related quality of life (HRQL) and health utility [10]. Patients with chronic HCV infection demonstrated lower HRQL compared with the general population. Recently, investigators have turned their interest to the impact of HCV infection on absenteeism, work force participation, and overall work impairment.

Even if patients are employed, the complete participation productivity may be limited. Worker productivity is measured through two key concepts: presenteeism and absenteeism. Absenteeism is related to the percentage of work time missed, while presenteeism is related to the percentage of impairment experienced at work time missed because of one's health [6].

To date, numerous studies have demonstrated the impact of HCV on health care costs. Previous studies have evaluated health care costs associated with HCV to be \$2470 per patient during the period from 1997 to 1999 [11, 12]. However, direct medical costs present only part of the societal burden of HCV infection. On the other hand, indirect costs related to work impairment have been ignored in the HCV literature for a long time. Previous models have omitted work impairment completely [13] or have evaluated productivity losses only in the premature mortality and disability as a consequence of projected late stage liver disease. Direct costs associated with HCV are fundamental. Also, indirect economic and humanistic costs are major and arise from the reduction of HRQL owing to both the disease and HCV treatments; this is related on the patient work, daily activities, and lifestyle [14].

Recent investigation has recognized a significant burden of HCV infection on work productivity, with infected patients missing 9% of working hours in the working week and reporting an average of 27% impairment while at work. Also, database study reported that HCV patients were 7.5% less productive based on work units per hour [15].

For better understanding of the societal impact of HCV, the association between the virus and work force participation and WP loss must be observed. It is also essential to investigate potential confusing variables that may contribute to a relationship between HCV and workplace activity. Nowadays, different studies have reviewed the impact comorbidities, and health behaviors may have on health outcomes among HCV patients, including psychiatric illness, fibrosis, fatigue, and depressive symptoms [16].

It would be educative and significant for some employers with a short-term focus to utilize a time series approach to document WP changes pre and post-HCV diagnosis. Although using a regression approach and a propensity scoring approach ensured a numerous series of results, other methodologies may be significant, especially when evaluating economic costs associated with HCV [16].

Patients with HCV infection have reduced WP, in terms of both presenteeism (impairment in WP while working) and absenteeism (productivity loss due to absence from work). The most important drivers of WP in HCV are impairment of physical aspects of PROs and clinical history of depression, anxiety, fatigue, and cirrhosis [4]. Some authors emphasize the impact of eradicating HCV virus on the WP of chronic HCV (CH-C) patients. Sensitivity analyses assessed the possibility that CH-C patients' labor costs were lower than the general populations and presented results by fibrosis stage. Before initiation of treatment, EU patients with CH-C genotype 1 (GT1) exhibited absenteeism and presenteeism impairments of 3.54 and 9.12%, respectively [17]. About 91.8% of EU patients in the ION trials achieved SVR and improved absenteeism and presenteeism impairments by 16.3 and 19.5%, respectively. Weighted average per-employed patient gains from treatment are projected to be higher in cirrhotic than in noncirrhotic patients. CH-C results in a significant economic burden to European society. Due to improvements in WP, sustained virologic response with treatment could provide substantial economic gains, partly offsetting the direct costs related to its widespread use [17].

HCV infection is generally considered an asymptomatic disease. However, studies have shown that HCV has a substantial negative impact on patients' quality of life and functioning. Su et al. [15] evaluated a total number of near 340,000 subjects. Workers with HCV had significantly more lost workdays per worker compared to the control cohort, including sick leave, short-term disability, and long-term disability. HCV-infected workers had 4.15 more days of absence per worker compared to the control cohort. Efficiency was measured by units of work processed per hour and workers with HCV processed 7.5% fewer units per hour than employees without HCV. All health care costs among HCV workers were significantly higher compared to the same costs among workers without HCV. This study provides evidence that there is a considerable secondary burden of disease and labels an association between HCV infection, efficiency, increased absenteeism, and higher health care benefit costs [15].

Gifford et al. [18] showed that at least 50% of the men had symptoms of HCV infection. Tiredness was the most common symptom, followed by nausea and pain in the liver. Men ignored symptoms of disease in higher percentage compared women. Thirty-five percent of men rated their health as 'fair' or 'poor' compared to 18% of men in the general population. Many were concerned about their ability to work and financial income, and more than half were worried about being unable to have a drink with their friends. Coughlan et al. presented a Dublin study documenting psychological well-being, mental health, and quality of life in 93 women diagnosed with medically acquired HCV infection. Overall, the women had significantly lower quality of life than the healthy female population. No significant difference was found between women who had a past or current HCV virus infection; they reported having low energy, poor health, and problems with work and other daily activities. Reduced quality of life can be related to the diagnostic process rather than HCV infection as such. While HCV have a significant physiological effect on the quality of life, it is imperative not to undervalue the social and psychological costs of being identified with a stigmatized chronic disease that has an unknown progression and outcome [19]. Gill et al. found that HCV compared to divorce, loss of source of income, or a move to another city diagnosis is a way more stressful. The authors suggested that pre-and post-test counseling and psychosocial support could help to decrease the stress related with HCV diagnosis [20]. HCV infection has a significant influence on the

quality of life. Not only do symptoms such as fatigue lessen effective functioning but also living with a chronic stigmatized disease with an indeterminate future creates problems around expose, retrieving care, and satisfying confidence, employment, and relations.

### **3. The impact of the HCV antiviral therapy on work ability**

A patient's ability to tolerate and adhere to HCV treatment has an impact to WP during the course of HCV treatment. This is important concern for patients considering treatment initiation because they will have to deal with the possibility of temporary reduced work participation during treatment [17].

Eradication of HCV may improve many different components of PRO, including HRQL and WP [21]. It is important that evaluation of new regimens for treatment of chronic hepatitis C (CHC) includes not only efficacy and safety reports but also data related to important PROs such as fatigue, HRQL, and WP [14]. The dual function of PRO is to represent patient experience with treatment and assess the indirect cost of treatment related to lower WP [22].

Treatment of HCV infection with the combination of peginterferon plus ribavirin (pegIFN/RBV) is a process with significant and sometimes dose-limiting adverse events. Those adverse effects further exacerbate the patient's already compromised productivity and consequently increase economic burden [17]. Brook et al. found that patients who received pegIFN/RBV took more sick leave, more long-term disability, and more workers' compensation than those without HCV treatment [3]. Perillo et al. designed a randomized control study and found that during treatment with peginterferon-alpha 2a, patients showed less impairment across all measures of work functioning and productivity when compared to patients who were treated with combination of interferon-alpha 2b plus ribavirin [23]. In a study conducted by McHutchison et al., randomly assigned patients who responded to therapy of IFN/RBV showed improvements across all measures of work functioning and productivity, in contrast with patients who received placebo. In addition, sustained responders work functioning and productivity decreased temporarily in approximately 46% of patients [14]. Patients who do not achieve an SVR are more likely to miss work or other commitments due to HCV infection or its treatment than those who achieve SVR. Aggrawal et al. confirmed that employed patients with genotype 1 chronic HCV infection receiving treatment have reduced work hours and reduced WP levels due to hepatitis or its treatment. This decline was observed early during the course of treatment, with return to baseline levels by week 72 post-treatment initiation, suggesting that WP losses can be considered a short-term outcome of HCV treatment [1].

To improve the tolerability and efficacy profile of anti-HCV treatment, a number of interferon-free regimens, such as sofosbuvir, have been developed. In a study by Younossi et al., subjects treated with the interferon-free regimen completely recovered by the end of 12 weeks of follow-up, their PRO scores returned to baseline values and showed further improvement. The impact on WP, especially presenteeism, was significantly more profound with the interferon-containing regimen than with the interferon-free regimen. Also, subjects who received the interferon-free regimen experienced substantially less fatigue compared with the subjects

receiving interferon-containing regimens [22]. Another study by Younossi et al. showed that interferon and ribavirin-free regimen are associated with significant gains in most aspects of HRQL during treatment regardless of the stage of liver disease [24]. Expanding the access to a highly effective cure for all HCV-infected patients will improve the clinical outcomes but also patient-reported outcomes such as HRQL and work productivity, resulting in a superlative comprehensive benefit to patients and society.

In conclusion, successful treatment and achieving SVR regardless of therapy have been associated with better economic outcomes [25]. For that reason, there is a strong evidence that this improvement can positively impact the indirect economic burden of HCV by improving WP.

#### 4. Conclusions

In general, work-related activities should not pose a risk to patient with chronic liver disease [26]. The exception would be:

1. Patients with hepatic encephalopathy for whom certain task such as driving and operating heavy machinery may be risky due to impaired judgment and cognitive defects.
2. Working with hepatotoxic chemical such as carbon tetrachloride, vinyl chloride, and polychlorinated biphenyls (PCBs).

Patients with advanced liver disease have decreased exercise capacity from anemia, ascites, renal failure, or hepato-pulmonary syndrome, and work limitations are advised [26].

Modifications to work and work ability assessment are required to prevent occupational transmission of HCV. This is usually only required in the health care setting, where infectious carriers of HCV should not carry out exposure-prone procedures (EPP). Even in an area with a high prevalence of HCV among its population, the risk of acquiring HCV through occupational exposure is low—the risk of an individual surgeon acquiring the HCV has been estimated at 0.001–0.032% per annum [26, 27]. Rates of viral clearance with treatment of acute HCV infection are considerably higher than treatment of chronic HCV infection. Consequently, it is imperative that health care workers follow universal precaution and promptly report all exposures to blood or body fluid exposures according to their local policy.

Health care workers who embark on, or transfer to, a career that requires EPP (exposure-prone procedures and dialysis work) should be assessed to ensure that they are free from infection with HCV. Members of staff known to have been exposed to the blood of a HCV-positive patient through sharps injury should continue to work normally, but it is necessary to do the following procedure [26] that is also shown at **Figure 1**:

1. HCV RNA polymerase chain reaction test 6 weeks after exposure.
2. Twelve weeks after exposure, HCV RNA polymerase chain reaction test should be taken again, together with HCV antibody testing.

3. Six months after exposure, additional HCV antibody testing should be commenced (repeated negative testing designates infection absence).

Those who have positive test results should stop undertaking EPPs instantly and should be taken as soon as possible for specialist assessment by a gastroenterologist and/or infectologist. Health care workers who already perform EPPs and who believe they may have been exposed to HCV infection should be advised to seek advice from their occupational health department for confidential advice on whether they should be tested.

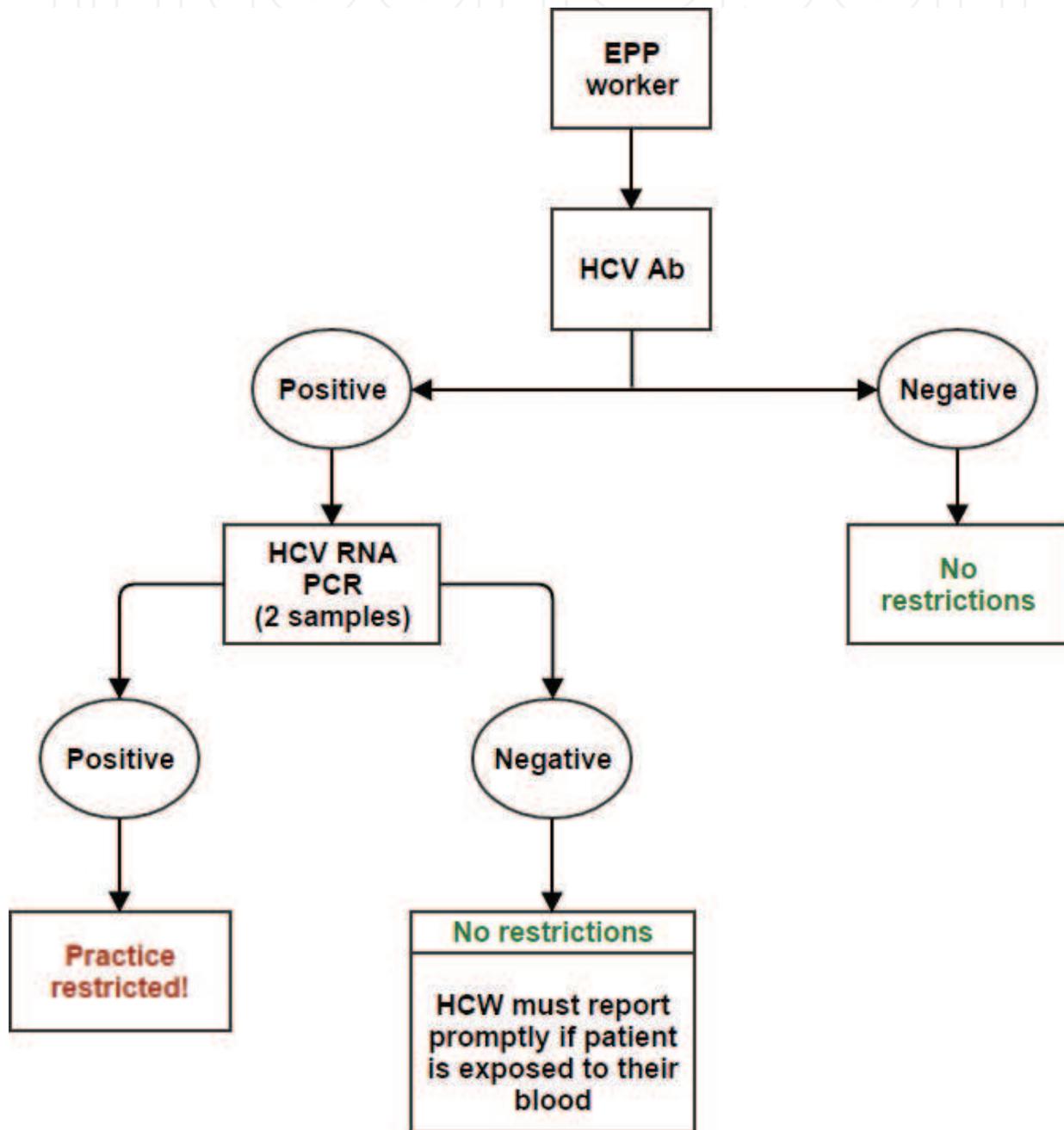


Figure 1. Investigation of HCV status in a worker performing exposure-prone procedures (Modified after Palmer et al. [26]).

Those health care workers who had HCV infection and have been treated with antiviral treatment may return to EPPs if they have tested negative to HCV RNA for at least 6 months after cessation of treatment. They should have one additional check for HCV RNA 6 months later. Present standard laboratory tests cannot demonstrate complete clearance of virus but can state that the virus is undetectable. In these situations, infectivity is likely to be so low that it is safe to return to EPPs and reactivation of infection is unlikely so no further testing is required. There is indication that infection remains within hepatocytes and can be reactivated following treatment with monoclonal antibodies (such as Rituximab) and other immunosuppressants (such as TNF- $\alpha$  inhibitors) including cancer chemotherapy. Recent data suggest that rituximab-based chemotherapy increases HCV expression in hepatic cells, can become a mark for a cell-mediated immune response after the treatment removal and the renewal of the immune control. Some studies have examined the incidence of HCV reactivation and related hepatic flare in patients with oncohematological diseases receiving R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone). These studies suggest that the hepatic flares are often asymptomatic, but life-threatening liver failure occurs in closely 10% of cases [28].

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